[redacted]

HFI-35 1505

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

D1230B

FOOD & DRUG ADMINISTRATION
466 FERNANDEZ JUNCOS AVENUE
SAN JUAN, P.R. 00901-3223

February 28, 1997

WARNING LETTER
SJN-97-07

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Christopher J. Conway
Chairman and Chief Executive Officer
Mentor Corporation
5425 Hollister Avenue
Santa Barbara, CA 93111

Dear Mr. Conway:

During an inspection of your firm, Mentor Caribe, Inc., located in Cidra, Puerto Rico, between 11/18/96 and 1/23/97, our Investigators determined that your firm manufactures various styles and models of intraocular lenses (IOL's) which are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act). At the conclusion of the inspection, a list of Inspectional Observations, FDA Form 483, was issued to Mr. Miguel Soler, Plant Manager. A copy of that FDA 483 is enclosed for your reference.

The subject inspection revealed that the above noted devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish, implement, and control written manufacturing specifications and processing procedures to assure that the device conforms to its original design or any approved changes in that design as required by 21 CFR 820.100. Examples include:

   a. Rejection rates exceeding specifications (Quality Index) for thin haptics in single piece IOL's were repeatedly observed during 1995 and 1996 for several models of modified and non-modified One-Piece IOL's. The rejection rates observed ranged from [redacted] to [redacted]% for the daily production during

several periods from 9/95 to 11/96, exceeding the firm's acceptance criteria for the daily production [redacted]. The individual work orders manufactured during these periods show rejection rates ranging from [redacted] t[redacted]

b. The validation of the blocking, lathing and milling operations used in the manufacture of One-Piece IOL's did not include evaluation of finished product performance. These operations were validated independently, using different work orders for the qualification and validation of each separate operation. The validations included only the results of inspections performed during the specific operation. The firm has not executed a validation protocol using the same work orders to validate all the manufacturing steps up to and including final product performance.

2. Failure to implement procedures adequate to assure the identification, recommendation or provision of solutions for quality assurance problems, and to verify the implementation of such solution as required by 21 CFR 820.20(a)(3). Examples include instances of thin haptic rejection rates exceeding the Quality Index action level of [redacted] which were not investigated, or for which investigations were deficient, or for which investigations have not been concluded or corrective actions completed after extended periods as cited on the FDA 483 including FIR (Failure Investigation Report) No. 96-0016, FIR No. 95-0027, FIR No. 950034, and all dates of production cited at Item No. 4 of the FDA 483. No complete explanation has been determined for the increase in rejection rates for thin haptics noted in the firm's records since September 1995. Nor has the firm thoroughly justified its failure to investigate the rejection rates cited in the daily work order records for those dates listed at Item No. 4. FIR 96-0016 has been open since March 1996 with no final resolution, or even complete implementation of interim corrective actions that have been identified.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close-out of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no pending applications for pre market approval (PMA's) or export approval requests will be approved and no pre market notifications (section 510(k)'s) will be found to be substantially equivalent for products manufactured at the facility in which the above GMP violations were found until the violations have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

We acknowledge that Ms. Maria Granito and Mr. David Downey of Mentor Ophthalmics submitted a written response, dated February 3, 1997, to this office concerning our investigators' observations noted on the form FDA 483 issued to Mentor Caribe, Inc. It appears that the response may adequately address corrective actions related to observations 6 through 13 of the FDA 483. However, final determination will depend upon future inspection results. Two areas of concern remain with regard to those specific observations:

1. The firm should address precisely how NIST traceability of calibration standards will be verified in future.

2. Observation by the inspectors of certain discrepancies in the records of calibration issued by the new calibration contractor indicate that Mentor should take special care to assure the work is done correctly. Specifically, the precision of data reported by the contractor in several instances did not seem to correlate with the available precision of the calibrating tools used, i.e. reporting measurements not consistent with available gauge sizes, and reporting to a level of decimal precision not available on the measuring instrument being calibrated. We presume this will be given thorough follow-up and appropriate steps will be taken by Mentor Caribe, Inc. to assure that equipment calibration is correctly accomplished and reported in the future.

We further acknowledge that a Mr. Rafael Pérez Cancel, Quality Assurance and Quality Control Manager, Mentor Caribe, Inc., submitted a second letter to this office, dated 2/13/97, in response to FDA 483 items 1 through 5, and 7. We are not satisfied that the comments contained in that letter adequately respond to the observations in Items 1 through 5. Of greatest concern is the incomplete validation of the manufacturing process. We acknowledge that the initial protocols were reviewed by the Center for Devices and Radiological Health. However, we are unconvinced that the implementation has been in accord with accepted good manufacturing practice. We further believe the deficient validation process may be related, among other things, to the inability of the firm's management to adequately explain the observed increase in process deviations for haptic thickness in single piece lenses. Changes in suppliers, procedures and equipment in use during production will almost always result in some change in process outcomes. The effects on process outcome are often unpredictable. Furthermore, failure to account for minor process changes at one processing step may unpredictably result in more significant outcome deviations downstream in the process.

The increased deviation rates for haptic thickness observed in the device history records for in-process inspection of single piece intraocular lenses manufactured by Mentor Caribe, Inc. indicate the existence of a significant and ongoing process instability of currently indeterminate cause. The various in-process inspections, and the one hundred percent final inspection of product may mitigate some of the effects of such a process problem, but cannot be accepted as a substitute for implementation of a properly validated, stable, and predictable manufacturing process. We recognize that all manufacturing processes are subject to some irreducible deviations. However, in order to demonstrate that your process has been validated, the rates of observed in-process defects may not be demonstrably increasing over time. Nor ought they to be subject to radical variability between work orders of like products.

We will continue our evaluation of Mr. Pérez's letter and may submit additional comment in future correspondence with your firm.

Please notify this office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. In formulating your reply, you may simply refer to the appropriate sections of prior correspondence from your firm insofar as that correspondence continues to reflect your policy. However, we would encourage supplementation of any responses which you believe require further clarification.

Your response should be sent to John M. McInnis, Compliance Officer, Food and Drug Administration, 466 Fernandez Juncos Ave., San Juan, PR 00901-3223.

Sincerely,

Samuel Jones
District Director

Enclosure:

FDA Form 483 issued 1/23/97

cc w/encl:
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